CLEAN VERSION OF REWRITTEN OR ADDED PARAGRAPHS

PURSUANT TO 37 C.F.R. § 1.121(b)(1)(ii)

1. On page 1 of the application as filed, after the "Title Of The Invention", please insert the following paragraph:

--PRIORITY

This application for patent under 35 U.S.C. 111(a) claims priority, under 35 U.S.C. § 119(e), to Provisional Applications Serial Numbers **60/141,156 (filed on 06/23/99) and 60/199,699 (filed on 04/26/00)**; wherein said Provisional Applications were filed under 35 U.S.C. 111(b).--

2. On page 1 of the application as filed, starting on line 4 (just before the paragraph beginning: "This invention was made on part with government support under grants. . .") please insert the following heading:

--STATEMENT REGARDING FEDERAL SPONSORSHIP--

3. In the specification, please replace the paragraph beginning on line 12 of page 5 with:

- -The present invention contemplates a composition comprising yeast with the relevant genotype of: *SUP7 ade2-1 can1-100 leu2-3 mod5-M2* and designated ALB1. The present invention further contemplates a composition wherein the yeast ALB1 is a strain of *Saccharomyces cerevisiae*. Still further, the present invention contemplates a composition comprising yeast with the relevant genotype of: *SUP7 can1-100 ade2-1 leu2-3 mod5::TRP1 ura3-1::MOD5* and designated ALB8. Even still further, the present invention contemplates a composition wherein the yeast ALB8 is a strain of *Saccharomyces cerevisiae*. Even further still, the present invention contemplates a composition comprising the yeast strain ALB1 wherein the genotype further comprises: *MATα mod5-M2 SUP7 ade2-1 can1-100 leu2-3, -112 lys1-1 lys2-1 trp1 ura3-1*. Even still further, the present invention contemplates a composition wherein the yeast ALB1 is a strain of *Saccharomyces cerevisiae*. Even further still, the present invention contemplates a composition comprising yeast with the relevant genotype of: *MATα SUP7 can1-100 ade2-1 leu2-3, -112 lys1-1 lys2-1 trp1 mod5::TRP1 ura3-1::MOD5*

and designated ALB8. Even further still, the present invention contemplates a composition of claim 7 wherein the yeast is *Saccharomyces cerevisiae*.- -

4. On page eight of the application as filed, please delete the following paragraphs (beginning on line 4):

"Figure 2 shows the level of isopentenylated tRNA found in ALB1 over-expressing *ERG20* is substantially reduced.

A. Low molecular weight RNA was prepared from ALB1 (*mod5-M2*) with each of the candidate genes or vector alone, ALB8 (*MOD5*) or MD14A (*mod5-1*). The RNAs were resolved on polyacrylamide gels, transferred to membranes and probed with anti-isopentenyl adenosine antibody (upper panel) or radiolabeled oligonucleotide complementary to mature $tRNA^{Tyr}$ (lower panel).

B. The levels of isopentenyl adenosine tRNA found in ALB1 with each of the candidate genes or vector only or in the strain ALB8 or MD14A were assessed by densitometric analysis of two immunoblots and expressed as a fraction of the level found in the "vector" control. (A) membrane 1 values; (B) membrane 2 values; (C) average values."

and insert:

- -Figure 2A is an autoradiograph. Low molecular weight RNA was prepared from ALB1 (*mod5-M2*) with each of the candidate genes or vector alone, ALB8 (*MOD5*) or MD14A (*mod5-1*). The RNAs were resolved on polyacrylamide gels, transferred to membranes and probed with anti-isopentenyl adenosine antibody (upper panel) or radiolabeled oligonucleotide complementary to mature $tRNA^{Tyr}$ (lower panel). This autoradiograph shows the level of isopentenylated tRNA found in ALB1 over-expressing *ERG20* is substantially reduced.

Figure 2B is a graph. This graph presents data showing the levels of isopentenyl adenosine tRNA found in ALB1 with each of the candidate genes or vector only or in the strain ALB8 or MD14A that were assessed by densitometric analysis of two immunoblots and expressed as a fraction of the level found in the "vector" control. (A) membrane 1 values; (B) membrane 2 values; (C) average

values. These data are also consistent with the finding that the level of isopentenylated tRNA found in ALB1 over-expressing *ERG20* is substantially reduced.- -

5. On page eight of the application as filed, please delete the following paragraph (beginning on line 16):

"Figure 3 presents a model of competition between i^6A modification of tRNA and sterol biosynthesis."

and insert:

- -Figure 3A presents a model of competition between i^6A modification of tRNA and sterol biosynthesis.

Figure 3B presents another model of competition between i^6A modification of tRNA and sterol biosynthesis.- -

6. On page eight of the application as filed, please delete the following paragraph (beginning on line 22):

"Figure 5 presents two yeast strains that present limited cytosolic levels of Mod5p. Cells with the mod5-M2KR6 allele (T8-ID with YCfmod5-M2KR6 as projected in Fig. 5) have a very small cytosolic pool of Mod5p and the cells are unable to grow in the absence of lysine."

and insert:

- -Figure 5A presents the growth characteristics for ALB1 cells and T8-1D cells (with YCfmod5-M2,KR6) under conditions of normal flux through the sterol biosynthesis pathway.

Figure 5B presents the growth characteristics for ALB1 cells and T8-1D cells (with YCfmod5-M2,KR6) under conditions such that flux through the sterol biosynthesis pathway is increased.

Figure 5C presents the growth characteristics for ALB1 cells and T8-1D cells (withYCfmod5-M2,KR6) under conditions such that flux through the sterol biosynthesis pathway is decreased.- -

7. In the specification, please replace the following paragraphs beginning on line 23 of page 9 and ending on line 33 of page 9 with:

- -Yeast strain "ALB1" is defined as a substantially pure population of yeast with the genotype of: *MATα mod5-M2 SUP7 ade2-1 can1-100 leu2-3, -112 lys1-1 lys2-1 trp1 ura3-1* and the relevant genotype of: *SUP7 ade2-1 can1-100 leu2-3-112 mod5-M2*. The yeast may be of the species *Saccharomyces cerevisiae*.

Yeast strain "ALB8" shall be defined as a substantially pure population of yeast with the genotype of: *MATα SUP7 can1-100 ade2-1 leu2-3, -112 lys1-1 lys2-1 trp1 mod5::TRP1 ura3-1::MOD5*. The yeast may be of the species *Saccharomyces cerevisiae*.

Yeast strain "T8-1D" shall be defined as a substantially pure population of yeast with the genotype of: *MATa SUP11 ade2-1 leu2-3, -112 mod5-1 lys2-1 his4-519 ura 3-1*. The yeast may be of the species *Saccharomyces cerevisiae*.- -

8. In the specification, please replace the paragraph beginning on line 24 of page 10 with:

- -The term "binding interaction" when used in relation to RNA shall be defined as the ability of two or more macromolecules to bind to each other (*e.g.*, to produce an aggregate). The present invention makes no limit on the stringency of the binding interaction so long as the interaction can be detected by methods known to those practiced in the art (*e.g.*, by Western blot, coimmunoprecipitation, spectrophotometry, colorimetric assay, etc.).- -

9. In the specification, please replace the paragraph beginning on line 18 of page 18 with:

- -ORF YDL219w is predicted to code for a 150 amino acid protein with no significant homology to any characterized protein. However two lines of evidence indicate that this protein may function in the translation process. First, the gene possesses an intron. As introns are rare in yeast other than for approximately half of the genes encoding ribosomal proteins (Woolford and Warner, in "The molecular and cellular biology of the yeast *Saccharomyces*: Genomic dynamics, protein synthesis and energetics" eds. Broach, *et al.* [Cold Spring Harbor Lab Press, Plainview, NY] Vol. 1, pp. 587-626, 1991), the presence of the intron is suggestive of a role in translation.

Second, Applicants show that over expression of YDL219w affects tRNA-mediated nonsense suppression.- -

10. In the specification, please replace the paragraph beginning on line 6 of page 32 with:

- -Library plasmids were isolated from yeast by the method of Ward (Ward, "Single-step purification of shuttle vectors favor yeast for high frequency back-transformation into *E. coli*" *Nucleic Acids Res* 18:5319, 1990). DNAs were sequenced by either the chain termination method (Sanger, *et al.*, "DNA sequencing with chain-terminating inhibitors" *Proc Natl Acad Sci USA* 74:5463-5467, 1977) with Psychognosy Version 2.0 DNA Sequencing Kit (United States Biochemical) or by automated cycle sequencing performed in the Pennsylvania State University College of Medicine Macromolecular Core Facility. Nucleotide sequences were identified by a BLAST (Altschul, *et al.*, "Basic local alignment search tool" *J Mol Biol* 215:403-410, 1990) search at the *Saccharomyces* Genome Database BLAST server.- -